quent AEs included dizziness, headache, and nausea or pharyngolaryngeal pain. Most of the AEs were mild in severity.

TABLE 21

Overview of Adverse Events - Safety Population

	Treatment			
	A PN 400 N = 38 n (%)	B EC Nap + EC Eso N = 39 n (%)	C EC Nap N = 39 n (%)	D EC Eso N = 39 n (%)
Subjects with at least 1 adverse event	3 (8)	6 (15)	1 (3)	2 (5)
Subjects with at least 1 serious adverse vent	0	0	0	0
Deaths	0	0	0	0
Withdrawals due to adverse events	0	0	0	0

EC = enteric-coated;

Nap = naproxen;

Eso = esomeprazole

A = PN 400 = naproxen 500 mg/esomeprazole 20 mg

B = EC Nap + EC Eso = enteric-coated naproxen 500 mg + enteric-coated esomeprazole 20 mg

C = EC Nap = enteric-coated naproxen 500 mg

D = EC Eso = enteric-coated esomeprazole 20 mg

AE data are summarized by system organ class (SOC) and provided in Table 22 below. The overall occurrence rate was notably greater with Treatment B (15%) than with the other treatments (3-8%). The only AEs occurring in more than 1 subject per treatment period were dizziness, which occurred in 2 subjects (5%) with Treatment B; headache, which occurred in 2 subjects with Treatment B; and pharyngolaryngeal pain, which occurred in 3 subjects (8%) with Treatment B.

TABLE 22

Treatment-Emergent Adverse Events - Safety Population

System Organ Class Adverse Event	A PN 400 N = 38 n (%)	B EC Nap + EC Eso N = 39 n (%)	C EC Nap N = 39 n (%)	D EC Eso N = 39 n (%)
Subjects with at least 1 adverse event	3 (8)	6 (15)	1 (3)	2 (5)
Nervous system disorders	2 (5)	3 (8)	0	2 (5)
Dizziness	1 (3)	2 (5)	0	1 (3)
Headache	0	2 (5)	0	1 (3)
Syncope	1 (3)	0	0	0
General disorders and administration site conditions	1 (3)	1 (3)	1 (3)	0
Chest discomfort	0	0	1 (3)	0
Cyst	1 (3)	0	0	0
Pain	0	1 (3)	0	0
Pyrexia	0	1 (3)	0	0
Respiratory, thoracic and mediastinal disorders	0	3 (8)	0	0
Pharyngolaryngeal pain	0	3 (8)	0	0
Cough	0	1 (3)	0	0
Gastrointestinal disorders	0	1 (3)	0	0
Nausea	0	1 (3)	0	0

TABLE 22-continued

Treatment-Emergent Adverse Events - Safety Population

System Organ Class Adverse Event	A PN 400 N = 38 n (%)	B EC Nap + EC Eso N = 39 n (%)	C EC Nap N = 39 n (%)	D EC Eso N = 39 n (%)
Injury, poisoning and procedural complications	1 (3)	0	0	0
Head Injury	1 (3)	0	0	0

EC = enteric-coated;

Nap = naproxen;

Eso = esomeprazole

A = PN 400 = naproxen 500 mg/esomeprazole 20 mg

B = EC Nap + EC Eso = enteric-coated naproxen 500 mg + enteric-coated esomeprazole 20 mg

C = EC Nap = enteric-coated naproxen 500 mg

D = EC Eso = enteric-coated esomeprazole 20

The only AEs assessed as treatment-related by the investigator were nausea, dizziness and headache in one subject and headache and pyrexia in another subject, each occurring during Treatment B.

What is claimed is:

1. A method for treating osteoarthritis, rheumatoid arthritis, or ankylosing spondylitis comprising orally administering to a patient in need thereof an AM unit dose form and, 10 hours (±20%) later, a PM unit dose form, wherein:

the AM and PM unit dose forms each comprises:

naproxen, or a pharmaceutically acceptable salt thereof, in an amount to provide 500 mg of naproxen, and

esomeprazole, or a pharmaceutically acceptable salt thereof, in an amount to provide 20 mg of esomeprazole;

said esomeprazole, or pharmaceutically acceptable salt thereof, is released from said AM and PM unit dose forms at a pH of 0 or greater,

the AM and PM unit dose forms target:

i) a pharmacokinetic (pk) profile for naproxen where:

a) for the AM dose of naproxen, the mean C_{max} is 86.2 μg/mL (±20%) and the median T_{max} is 3.0 hours (±20%); and

b) for the PM dose of naproxen, the mean C_{max} is 76.8 μg/mL (±20%) and the median T_{max} is 10 hours (±20%); and

ii) a pharmacokinetic (pk) profile for esomeprazole where:

a) for the AM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the AM dose is administered to 10 hours (±20%) after the AM dose is administered ($AUC_{0-10,am}$) is 1216 hr*μg/mL (±20%),

b) for the PM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the PM dose is administered to 14 hours (±20%) after the PM dose is administered ($AUC_{0-14,pm}$) is 919 hr*μg/mL (±20%), and

c) the total mean area under the plasma concentration-time curve for esomeprazole from when the AM dose is administered to 24 hours (±20%) after the AM dose is administered (AUC_{0-24}) is 2000 hr*μg/mL (±20%); and

the AM and PM unit dose forms further target a mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state that is at least about 60%.